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Central venous thrombosis in children with intestinal failure on long-term parenteral nutrition☆,☆☆

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ABSTRACT

Purpose: Central venous thrombosis (CVT) is a serious complication of long-term central venous access for parenteral nutrition (PN) in children with intestinal failure (IF). We reviewed thse incidence of CVT and possible risk factors.

Methods: Children with IF on home PN (2010–2014) with central venous imaging were reviewed. Patient demographics, catheter characteristics and related complications, and markers of liver function were compared between children with and without CVT. Serum thrombophilia markers were reviewed for patients with CVT.

Results: Thirty children with central venous imaging were included. Seventeen patients had thrombosis of ≥1 central vein, and twelve had ≥2 thrombosed central veins. Patients with and without CVT had similar demographics and catheter characteristics. Patients with CVT had a significantly lower albumin level (2.76 ± 0.38 g/dL vs. 3.12 ± 0.41 g/dL, $p = 0.0223$). The most common markers of thrombophilia in children with CVT were antithrombin, protein C and S deficiencies, and elevated factor VIII. There was a statistically significant correlation between a combined protein C and S deficiency and having >1 CVT.

Conclusions: Children with IF on long-term PN are at high risk for CVT potentially owing to low levels of natural anticoagulant proteins and elevated factor FVIII activity, likely a reflection of liver insufficiency and chronic inflammation.

Children with intestinal failure (IF) are dependent on intravenous fluids and parenteral nutrition (PN), often for a prolonged period of time, for normal growth and development [1]. A functional central venous catheter (CVC) is therefore essential to their survival until intestinal adaptation occurs. Despite many advances in the nutritional management of children with IF, catheter-related complications still represent significant morbidity. The most common complications directly related to central venous access include infection and catheter occlusion and/or malfunction [2–4]. Children with intestinal failure tend to be at particularly high risk for CVC-related complications because

Abbreviations: CVT, central vein thrombosis; PN, parenteral nutrition; IF, intestinal failure; CVC, central venous catheter; CLABSI, central line associated bloodstream infection.

☆ Author's RoleJessica Gonzalez-Hernandez, MD, made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data for the work; drafted the work and revised it critically for important intellectual content; gave final approval of the version to be published; and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.Yahya Daoud, MSc, made substantial contributions to the interpretation of data for the work; gave final approval of the version to be published; and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.Jennifer Styers, CPNP, made substantial contributions to the acquisition of data for the work, and is in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.Janna M. Journeycake, MD, made substantial contributions to the conception and design of the work, gave final approval of the version to be published; and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.Nandini Channabasappa, MD, made substantial contributions to the conception and design of the work, gave final approval of the version to be published; and is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.Hannah G. Piper, MD, made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data for the work; drafted the work and revised it critically for important intellectual content; gave final approval of the version to be published; and is in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

☆☆ Level of Evidence: 2b.

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Table 1
Patient demographics.

Parameters	Children without thrombosis (n = 13)	Children with thrombosis (n = 17)	*P* value
Gestational age (mean ± SD, weeks)	34.5 ± 3.5 (range 27–40)	31.7 ± 5.2 (range 23–38)	0.0868
Age (years)	3.2 ± 4.2	3.7 ± 4.6	0.7647
Gender (males, %)	46	35	0.7106
Diagnosis (%)			
Necrotizing enterocolitis	8	35	
Atresia	46	18	
Gastroschisis	0	29	0.0240*
Omphalocele	0	0	
Volvulus	31	12	
Hirschsprung disease	0	0	
Other	15	6	
Small bowel length (mean ± SD, cm)	34.8 ± 13.6	47.7 ± 55.5	0.4003
Expected small bowel based on gestational age (mean ± SD, %)	31.5 ± 23.8	41.3 ± 31.6	0.3545

SD, standard deviation.
* $P < 0.05$.

the catheters are used frequently, usually on a daily basis, for prolonged periods of time and the patients often have some degree of chronic inflammation [5]. Central venous thrombosis (CVT), another significant complication, has been less well studied in this patient population. The prevention of CVT has become increasingly important as more children with IF are surviving infancy and are sustained on long-term PN. The loss of access sites owing to thrombosis can seriously complicate the ability to provide PN and even jeopardize transplant eligibility [6,7]. The true incidence of central vein thrombosis is not well known partly because children with CVT are often asymptomatic and therefore detection requires active screening, which is not commonly done. Previous studies have identified the size and location of the CVC, the delivery of PN, and bloodstream infections as possible risk factors for CVT, however this has not been well defined for these patients [8–10]. The purpose of this study is to determine the incidence of CVT and potential risk factors for children with IF on long-term PN.

1. Methods

1.1. Study population

After obtaining approval from the University of Texas Southwestern Investigational Review Board, a retrospective review of children with intestinal failure treated by the Center for Intestinal Rehabilitation at Children's Health from January 2010 through December 2014 was performed. Only children with intestinal failure treated with home parenteral nutrition for greater than 3 months and who had documented central venous imaging were included. Central venous imaging was obtained based on surgeon preference in preparation for catheter placement. None of the children had symptoms prompting imaging. Central venous imaging consisted of either a venous Doppler ultrasound or magnetic resonance venography. The children with and without documented CVT were compared.

1.2. Data collection

Patient demographics such as age, gender, diagnosis, small bowel length and percentage of expected small bowel based on gestational age were collected. Within the group of patients with CVT, the number and location of thrombosed veins were also assessed. Catheter-related information (days on parenteral nutrition, number of catheters per patient, catheter diameter, number of central line associated bloodstream infection (CLABSI) per 1000 catheter days and number of catheter occlusions per 1000 catheter days), and liver enzymes/markers of hepatic function (ALP, AST, ALT, GGT, total and direct bilirubin, INR, albumin, platelet count) were compared between patients with and without CVT. Serum markers of thrombophilia were also evaluated for the majority of those with CVT.

1.3. Statistical analysis

Descriptive statistics were reported in terms of means, standard deviations, ranges, proportions and frequencies as applicable. Statistical testing of subgroups included chi-square test and ANOVA, as appropriate to the variable's level of measurement and distribution using JMP by SAS. A *P* value of <.05 was considered significant.

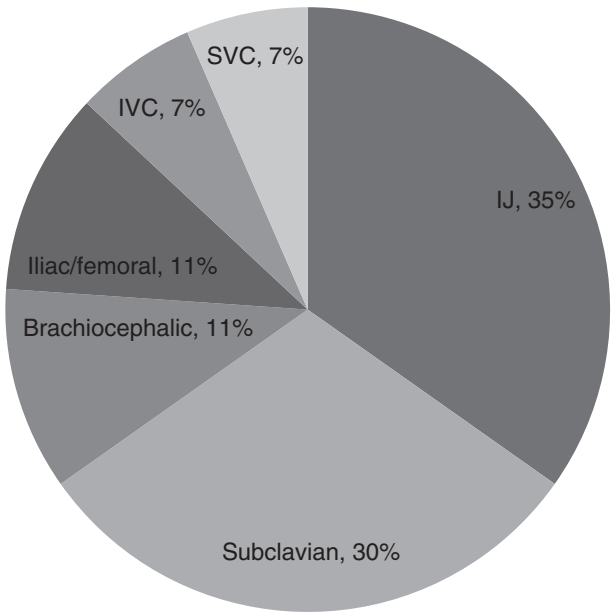

Fig. 1. Percentage of thrombosed central veins based on location in children with intestinal failure.